

WHAT IS CLAIMED IS:

1. A synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes a mammalian heparanase protein, the sequence of nucleotides comprising two consensus cleavage sites recognized by an endoproteinase, the cleavage sites located between nucleotides encoding residues 100 and 168 of the heparanase protein.
2. A vector comprising the nucleic acid molecule of claim 1.
3. The vector of claim 2, wherein the vector is a baculovirus vector.
4. A host cell comprising the vector of claim 3.
5. The host cell of claim 4, wherein the host cell is an insect cell.
6. The host cell of claim 4, wherein the host cell is a yeast cell.
7. The host cell of claim 6, wherein the yeast is selected from the group consisting of: *Pichia pastoris*, *Hansenula polymorpha* and *Saccharomyces cerevisiae*.
8. The synthetic nucleic acid molecule of claim 1, wherein the heparanase protein is human heparanase.
9. The synthetic nucleic acid molecule of claim 8, wherein the consensus cleavage sites are located before residues G110 and K158 of the human heparanase protein.
10. The synthetic nucleic acid molecule of claim 8, wherein the consensus cleavage sites are selected from the group consisting of: tobacco etch virus (TEV) protease cleavage sites, 3C protease cleavage sites from picornavirus, thrombin protease cleavage sites, enterokinase cleavage sites and factor Xa cleavage sites.
11. A synthetic mammalian heparanase nucleic acid molecule comprising a portion that encodes a mammalian heparanase protein, the protein coding portion consisting essentially of a sequence of nucleotides encoding an N-terminal fragment of about 8 kDa, a linker, and a sequence of

nucleotides encoding a C-terminal fragment of about 50 kDa, wherein the N-terminal and C-terminal fragments encode protein fragments that are substantially similar to wild-type heparanase fragments, and wherein the encoded heparanase protein is constitutively active.

- 5 12. The gene of claim 11, wherein the protein coding portion encodes human heparanase.
13. The gene of claim 11, wherein the linker comprises a sequence of nucleotides that encodes a central loop region of the hyaluronidase protein.
- 10 14. The gene of claim 13, wherein the hyaluronidase is from *H. manillensis*.
15. The gene of claim 12, wherein the linker comprises a sequence of nucleotides that encodes a (GlySer)₃ linker.
- 15 16. A vector comprising the gene of claim 12.
17. A host cell comprising the vector of claim 16.
- 20 18. The host cell of claim 17 which is an insect cell or a yeast cell.
19. A purified synthetic heparanase protein encoded by the gene of claim 12.
20. A method of expressing mammalian heparanase in non-mammalian cells
- 25 comprising:
- (a) transforming or transfecting non-mammalian cells with a vector comprising a sequence of nucleotides that encodes a mammalian heparanase protein, the sequence of nucleotides comprising two consensus cleavage sites recognized by an endoproteinase, the cleavage sites located between residues 100 and 168 of the heparanase protein;
- 30 (b) culturing the host cell under conditions which allow expression of said heparanase protein;
- (c) disrupting the cells and at least partially purifying the heparanase protein; and
- (d) exposing the at least partially purified heparanase protein to the endoproteinase, wherein the heparanase protein is cleaved at the consensus cleavage sites.

21. A method as in claim 20, wherein the heparanase is human.

5 22. A method of expressing a single chain, constitutively active mammalian heparanase in non-mammalian cells comprising:

(a) transforming or transfecting non-mammalian cells with a vector comprising a synthetic mammalian heparanase gene, wherein the synthetic gene comprises a portion that encodes the heparanase protein, the protein coding portion consisting essentially of a sequence of nucleotides encoding an N-terminal fragment of about 8 kDa, a sequence of nucleotides encoding a linker and a
10 sequence of nucleotides encoding a C-terminal fragment of about 50 kDa, wherein the N-terminal and C-terminal fragments encode protein fragments that are substantially similar to wild-type fragments; and
(b) culturing the host cell under conditions which allow expression of said heparanase protein

15 23. The method of claim 22 wherein the linker comprises a central loop region of the hyaluronidase protein.

24. The method of claim 22 wherein the linker comprises a central (GlySer)₃.

20 25. A substantially pure protein produced by the method of claim 22.